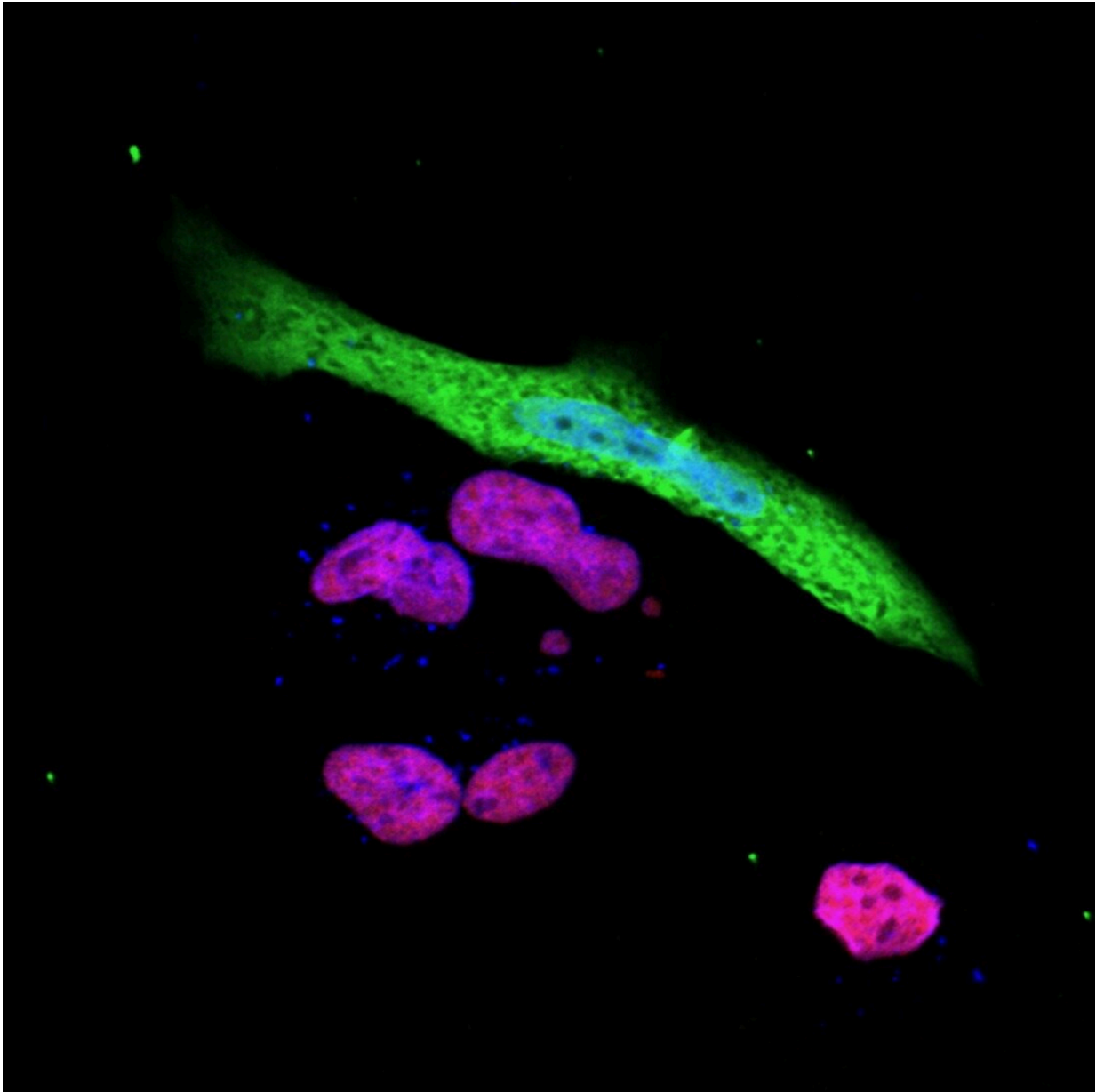


# How SARS-CoV-2 evades the immune system

December 7 2021

---



The expression of the immune response gene NLRC5 (red purple) is suppressed

in SARS-CoV-2 (green) infected cells (Photo: Koichi Kobayashi). Credit: Koichi Kobayashi

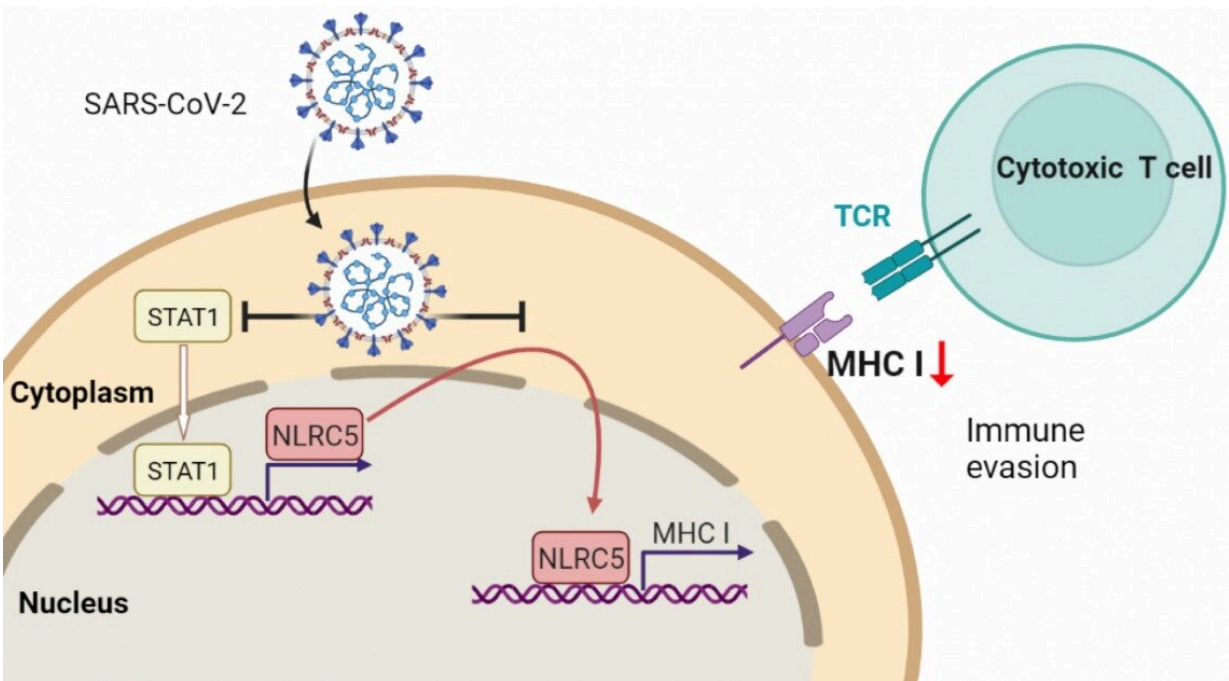
Researchers in Japan and the United States have found SARS-CoV-2 can knock out an important molecular pathway linked to an immune complex called MHC class I. The finding should help scientists better understand how COVID-19 infection takes hold.

"Our discovery reveals how the virus can evade the human immune defense system and might help to explain why the pandemic has been so severe," says Hokkaido University and Texas A&M University immunologist Koichi Kobayashi, who led the study. "The mechanisms we identify may provide new molecular targets for [drug discovery](#)."

The scientists used a bioinformatics approach to look at how SARS-CoV-2, the virus that causes COVID-19, changes gene expression in the immune systems of COVID-19 patients compared to uninfected individuals. This is a useful way to look into the function of complicated cell signaling pathways that trigger immune responses to fight off harmful bacteria and viruses.

MHC (major histocompatibility complex) class I molecules are a central weapon in the [immune response](#) against viruses. When a virus infects a cell, the cell facilitates the expression of viral antigens on the surface of [infected cells](#), drawing the attention of immune cells called cytotoxic T cells. These [immune cells](#) zero in on and destroy the infected cells, together with the invading virus inside them.

In addition to analyzing gene expression in COVID-19 patients, the research team also infected human cell lines with the SARS-CoV-2 virus to validate their findings.



SARS-CoV-2 escapes from immune responses by cytotoxic T cells via impaired MHC-I expression which is caused by reducing both the amount and function of NLRC5. Credit: Koichi Kobayashi

The results showed that a protein from the SARS-CoV-2 virus, called ORF 6, suppresses a host cell protein, called NLRC5, responsible for activating the MHC class I pathway.

The study showed this happens in two ways. ORF6 hampers cell signaling, which turns off the expression of NLRC5. ORF6 also blocks the function of NLRC5.

Other infectious viruses, including HIV and MERS, are known to also target the MHC class I pathway. Researchers believed that SARS-CoV-2 probably did as well, but this study is the first to unravel the mechanism.

"Without the activation of the MHC class I pathway, viruses in the infected cells are essentially hidden from the immune system. That helps to explain why SARS-CoV-2 virus persists in the body and why it keeps infecting others, leading to the pandemic," Kobayashi says.

Further research could help find and test drugs that block the activity of the ORF6 viral protein, to restore host cell ability to activate the major histocompatibility complex. If successful, such drugs could encourage the host immune system to clear the virus itself, effectively boosting immune responses.

**More information:** Ji-Seung Yoo et al, SARS-CoV-2 inhibits induction of the MHC class I pathway by targeting the STAT1-IRF1-NLRC5 axis, *Nature Communications* (2021). [DOI: 10.1038/s41467-021-26910-8](https://doi.org/10.1038/s41467-021-26910-8)

Provided by Hokkaido University

Citation: How SARS-CoV-2 evades the immune system (2021, December 7) retrieved 28 April 2024 from <https://medicalxpress.com/news/2021-12-sars-cov-evades-immune.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--